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FAX TRANSMISSION

To	USPTO
Examiner	Rebecca L. Anderson
Fax Number	(571) 273-8300
From	Daniel A. Pearson
Date	August 30, 2006
Application No.	10/626,356
Attorney Docket No.	VPI/00-122 DIV2 US
	Petition to the Director to Withdraw Finality of Office Action
Total Pages	32

Message or Comment

If any problems occur with this fax transmittal, please call (617) 444-6790 immediately.

Attorney Docket No.: 00-122 DIV2 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.:	10/626,356
Confirmation No.:	1551
Filing Date:	July 24, 2003
Examiner:	Rebecca Anderson
Group Art Unit:	1626
Applicants:	Michael Hale et al
For:	ISOXAZOLE COMPOSITIONS USEFUL AS INHIBITORS OF ERK

August 30, 2006
Cambridge, Massachusetts

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of Facsimile Transmission Under 37 CFR §1.8

I hereby certify that this correspondence and any documents referred to as attached hereto are being facsimile transmitted to the United States Patent and Trademark Office on August 30, 2006.

Lisa M. Romano

Signature

TRANSMITTAL LETTER

Sir:

Transmitted herewith: [X] a Petition to the Director to Withdraw Finality of Office Action; [X] a copy of the 7/25/06 Office Action; [ ] a Declaration; [ ] a Power of Attorney; [ ] a copy of a Notice to File Missing Parts; [ ] a Response to Notice to File Missing Parts; [ ] a Supplemental Declaration; [ ] an Associate Power of Attorney; [ ] a substitute Specification; [ ] formal drawings; [ ] Notice of Appeal; [ ] Appeal Brief; [ ] Petition for Revival; to be filed in the above-identified patent application.

Applicants: Michael Hale et al.
Application No. 10/626,356

FEE FOR ADDITIONAL CLAIMS

[X] A fee for additional claims is not required.

[ ] A fee for additional claims is required.

The additional fee has been calculated as shown below:

CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE		ADDITIONAL FEES
TOTAL CLAIMS	-		* =	X		$ 50	=	$ 0
INDEPENDENT CLAIMS	-		** =	X		$200	=	$ 0
FIRST PRESENTATION OF A MULTIPLE DEPENDENT CLAIM				+		$360	=	$
				TOTAL				$ 0

* If less than 20, insert 20.
** If less than 3, insert 3.

[ ] A check in the amount of $___ in payment of the filing fee is transmitted herewith.

[ ] Please charge $___ to Deposit Account No. 50-0725 in payment of the filing fee. A duplicate copy of this transmittal letter is transmitted herewith.

[X] The Director is hereby authorized to charge payment of any additional filing fees required under 37 C.F.R. § 1.16, in connection with the paper(s) transmitted herewith, or credit any overpayment of same, to deposit Account No. 50-0725. A duplicate copy of this transmittal letter is transmitted herewith.

Applicants: Michael Hale et al.
Application No. 10/626,356

EXTENSION FEE

[ ] The following extension is applicable to the Response filed herewith; [ ] $120.00 extension fee for response within first month pursuant to 37 C.F.R. § 1.136(a); [ ] $450.00 extension fee for response within second month pursuant to 37 C.F.R. § 1.136(a); [ ] $1,020.00 extension fee for response within third month pursuant to 37 C.F.R. § 1.136(a); [ ] $1,590.00 extension fee for response within fourth month pursuant to 37 C.F.R. § 1.136(a); [ ] $2,160.00 within fifth month pursuant to 37 C.F.R. § 1.136(a).

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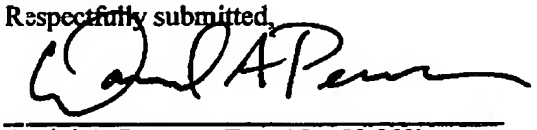
MISCELLANEOUS FEES

[ ] Please charge $_____ to Deposit Account No. 50-0725 in payment of the for _____ (37 C.F.R. §_____).

Respectfully submitted,



Daniel A. Pearson (Reg. No. 58,053)
Agent for Applicants
Karen E. Brown (Reg. No. 43,866)
Attorney for Applicants
c/o Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
Tel: (617) 444-6790
Fax: (617) 444-6483
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Attorney Docket No.: 00-122 DIV2 US

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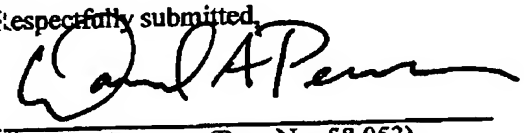
Respectfully submitted,



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August 30, 2006
Cambridge, Massachusetts

Mail Stop Petition
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PETITION TO THE DIRECTOR UNDER C.F.R. § 1.181 TO WITHDRAW FINALITY OF OFFICE ACTION

Sir:

Pursuant to 37 C.F.R. § 1.181 (a), applicants hereby petition to withdraw the finality of the July 25, 2006 Office Action (hereafter, "the final action"). Under the Manual of Patent Examining Procedure (MPEP) § 706.07(c), any question as to the prematureness of a final rejection should be raised while the application is still pending before the primary examiner. Further, this petition is filed within two months of the final action. Thus, this action is timely filed. See 37 C.F.R. § 1.181 (f).

Statements of Facts

The Examiner, Rebecca Anderson, issued a restriction requirement in the above-identified application that restricted compounds of the invention (Group I) from the methods of using these compounds (Group II). Applicants elected Group I. Subsequently, Examiner Anderson issued a non-final Office action rejecting the compound claims. Examiner Anderson did not examine the methods of Group II in the non-final Office action. Applicants filed an amendment and response to the non-final Office action. In the subsequent Office action, which was made final, Examiner Anderson found the claims of elected restriction Group I to be allowable and rejoined the withdrawn claims of restriction Group II. Examiner Anderson then rejected the rejoined claims under 35 U.S.C. § 112, and made the action final, stating that the amendment of the claims of Group I "necessitated the new ground(s) of rejection presented in [the] Office action." See the attached final action.

A telephonic interview was conducted between applicants and Examiner Anderson on July 31st, at which time Examiner Anderson stated that making an action final after rejoinder in the same Office action is standard USPTO policy if the rejoinder is the result of claim amendment of the originally examined claims. It is the Examiner's assertion that rejection of the rejoined claims is properly made final under MPEP § 706.07(a), which states, in part:

> Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement.

During a second telephonic interview conducted on August 3rd with Examiner Anderson and Supervising Examiner Joseph McKane, Examiner McKane confirmed that Examiner Anderson accurately articulated the policy. In the inverview, Examiner McKane also referenced a 2004 USPTO policy memo from the technology center directors to the examining corps stating that this was standard policy.

Argument in Support of Petition

Applicant hereby petitions to have the finality of the July 25, 2006 Office action withdrawn for the following reasons:

I. The policy stated by Examiners Anderson and McKane of finally rejecting newly rejoined claims is an incorrect interpretation of the MPEP.

> Before final rejection is in order ***a clear issue should be developed between the examiner and applicant***. To bring the prosecution to as speedy conclusion as possible and at the same time to deal justly by both the applicant and the public, the invention as disclosed and claimed should be thoroughly searched in the first action and ***the references fully applied***....In making the final rejection, all outstanding grounds of rejection of record should be carefully reviewed, and any such grounds relied on in the final rejection ***should be reiterated***. [§ 706.07, emphasis added]

In the prosecution of the instant application, no references were applied to the claims of Group II in the first Office action, as the references used in the rejection of the Group II claims in the final action were used for the first time. In addition, the grounds for rejection of the claims of Group II were not reiterated, since the rejection of these claims was made for the first time in the final action. Thus, a clear issue between the Examiner and applicants regarding the claims of Group II was never developed because the claims of Group II had not been examined until the final action.

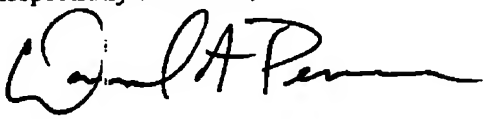
II. A final action unfairly limits applicants' options in proceeding with this case. Under 37 C.F.R. § 1.116, a claim amendment made after a final rejection must either (i) cancel the rejected claims, (ii) comply with any requirement or form set forth in a previous Office action, (iii) present the rejected claims in better form for consideration on appeal, or (iv) comply with the rules established for a Request for Continued Examination (RCE) under 37 § C.F.R. 1.114. Although an amendment and reply may be entered and considered after a final rejection, examination of such an amendment is entirely at the examiner's discretion. In the final action, the Examiner's only guidance is that the rejection can be overcome by cancellation of the newly rejoined method claims of Group II. Therefore, if an after-final amendment is filed in the instant application that does not cancel the claims of Group II, there is no guarantee that the amended claims will be examined unless they are considered under appeal or an RCE is filed.

Given the limited number of options after issuance of a final action and the mandates of USPTO policy as articulated by Examiners Anderson and McKane, applicants, through no fault of their own, are likely to have to file an RCE or an appeal to ensure that the scope of the claims of Group II are commensurate with their invention. This is unjust to the applicants because either an RCE or an appeal wastes valuable time in the prosecution or appeal process and money in the fees required for their filings. Filing an RCE or having the rejected claims considered on appeal also uses up valuable USPTO time and resources, as any continued examination or appeals process almost certainly will require more effort from the Office than fully developing the issue in the instant application through issuance of a non-final Office action.

III. The coupling of a final Office action with the removal of any restriction group distinction between the claims of Groups I and II puts applicants at a disadvantage should any of the claims of Group II be canceled and appear later in a divisional application. As stated in the final action, "applicant(s) are advised that if any claims including all the limitations of an allowable product claim or rejoined process claim are presented in a continuation or divisional application, such claims may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application." Thus, applicants are left with the possibility of having to terminally disclaim their patent in order to ensure that they will have patent protection on the methods of Group II commensurate in scope with their invention. Even if such a rejection is not made in an Office action and the hypothetical divisional application matures into a patent, the claims of Group II could be attacked during litigation, where their validity could be questioned using similar double-patenting arguments against them. For these reasons, applicants believe that should the Examiner's suggestion of overcoming the rejection in the final action by canceling the claims of Group II be followed, the status of these claims in future applications or patents would be compromised.

For the above reasons, applicants respectfully request that the Commissioner consider the matters taken up in the arguments and withdraw the finality of the July 25, 2006 Office action under MPEP § 706.07(d).

Respectfully submitted,



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,356	07/24/2003	Michael R. Hale	VPI/00-122 DIV2 US	1551

27916 7590 07/25/2006

VERTEX PHARMACEUTICALS INC.
130 WAVERLY STREET
CAMBRIDGE, MA 02139-4242

EXAMINER	
ANDERSON, REBECCA L	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 07/25/2006

MAILED

Final Office action 10/25/06
with 3 Ext - 1/25/07
Notice of Appeal - 1/25/07

Please find below and/or attached an Office communication concerning this application or proceeding.

RECEIVED
JUL 27 2006
7/27/06
VERTEX PHARMACEUTICALS INC.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/626,356	HALE ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,18-23 and 27-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-13 and 18-22* is/are allowed.

6)☒ Claim(s) *23 and 27-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13, 18-23 and 27-41 are currently pending in the instant application. Claims 1-13 and 18-22 appear allowable over the prior art of record and claims 23 and 27-41 are rejected.

Election/Restrictions

Claims 1-13 and 18-22 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 23 and 27-41 directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, the restriction requirement between Groups I and II as set forth in the Office action mailed on 31 January 2005 is hereby withdrawn. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claims including all the limitations of an allowable product claim or rejoined process claim are presented in a continuation or divisional application, such claims may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Response to Amendment and Arguments

Applicant's amendment and arguments filed 16 May 2006 have been fully considered. Applicants' amendment to claims 1 has overcome the objection to claim 1. Applicants' arguments in regards to the objection to claims 5, 9 and 13 are considered persuasive and the objection is withdrawn as claims 5, 9 and 13 are not substantial duplicates of the claims from which they depend. As the claims from which claims 10 and 13 depend appear allowable, the objection to claims 10-13 as being dependent upon a rejected base claim is withdrawn. Applicants' amendment to claim 18 has deleted the non-elected subject matter from the claim and has overcome the objection to claim 18 and the 112 2nd paragraph rejection of the claim. The amendment to claims 21 and 22 has overcome the 35 USC 112 1st paragraph rejection of these claims. As US Application No. 10/919,774 has been abandoned, the provisional obvious type double patenting rejection is overcome. Additionally, the premature 35 USC 103(a) rejection based on 35 USC 102(f) of the claims with US Patent Application No. 10/919,774 is also overcome as US Patent Application No. 10/919,774 has been abandoned and there is no evidence that the conflicting inventions were not commonly owned at the time the invention in this application was made. Lastly, as US Patent Application No. 10/919,774 is no longer a copending application and has been abandoned, applicant need not provide a showing that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23 and 27-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of claims 23 and 27-41 is the method of inhibiting ERK or AKTa ctivity in a biological sample and the treatment of a disease such as cancer, stroke, diabetes, hepatomegaly, cardiovascular disease, Alzheimer's disease, cystic fibrosis, viral disease, autoimmune diseases, atherosclerosis, restenosis, psoriasis, allergic disorders, inflammation, neurological disorders, a hormone-related disease, conditions associated with organ transplantation, immunodeficiency disorders, destructive bone disorders, proliferative disorders, infectious diseases, conditions associated with cell death, thrombin-induced platelet aggregation, chronic myelogenous leukemia (CML), liver disease, or pathologic immune conditions involving T cell activation. Furthermore, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of the above listed diseases, whether or not the disease is effected by the inhibition of AKT and ERK would make a difference.

Applicants are claiming methods which include the treatment of various diseases such as cardiovascular disease, stroke, inflammation, cancer, Alzheimer's disease, viral infection (which includes HIV), etc.

Applicants' claims are therefore drawn to the treatment of Alzheimer's disease. It is the state of the art that there is no known cure or prevention for Alzheimer's disease and that there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease. (URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html.

Furthermore, Layzer, Cecil Textbook of Medicine (article enclosed), states that "some degenerative diseases are difficult to classify because they involve multiple

anatomic locations" (see page 2050). Alzheimer's disease has traditionally been very difficult or impossible to prevent or event o treat effectively with chemotherapeutic agents. See e.g., the Cecil Textbook of Medicine, 20th edition (1996), Vol. 2, wherein it is stated that "[t]here is no cure for Alzheimer's disease, and no drug tried so far can alter theh progress of the disease" (pg. 1994).

In regards to the treatment of inflammatory disorders, enablement for the scope of treating inflammatory disorders generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually in any part of the body. There is a vast range of forms that in can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilation and leaking of vessels, and recruitment of circulating neurophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells.

Granulomas are seen in certain chronic inflammation situations. There are clusters of macrophages, which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation of the bladder, usually caused by bacteria, Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasoacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulites is inflammation of the tissues around the eye, and Orbital cellulites is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise form staphylococcus. Hence, these types of inflammations are treated with antibiotics. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to accept any agent to be able to treat inflammation generally.

In regards to the treatment and prevention of various cardiovascular disorders, "Cardiovascular disorders" embrace a vast array of problems, many of which are contradictory to others. Thus, it covers hypertension and hypotension. It covers various types of arrhythmias; angina pectoris', the thrombotic symptoms of diabetes,

atherosclerosis and hyperlipoproteinaemias, ischemic heart disease including congestive heart failure and myocardial infarction, stroke, and peripheral vascular disorders, such as deep-vein thrombosis, elevated blood levels of triglycerides, of total cholesterol or of LDL cholesterol, arteriosclerosis, peripheral vascular disease, cerebral vascular disease and pulmonary hypertension, migraine, cardiomyopathy, etc. Not one compound, let alone a genus of compounds, could possibly be effective against such disorders generally.

Stroke represents one of the most intractable medical challenges. Stroke is estimated to cause about 15% of deaths. Even those who survive normally suffer from persistent damage, including motor and speech disturbances and/or convulsions. Despite a tremendous effort to resolve these problems, cerebrovascular therapy as so far been limited to trying to prevent further damage in areas on the margins of the ischemic focus, this trying to maintain adequate perfusion in remaining intact areas, and thereby limit progressive infarction. This is generally done surgically. Standard pharmaceutical treatment, such as antiarrhythmics and antithrombotics don't get at the cause of the stroke or the damage caused, but are mostly done to insure adequate cardiac functioning.

Applicants are claiming compounds useful in medical therapy which includes the treatment of for example, HIV infection. As such, the specification fails to enable the skilled artisan to use the compounds of the formula (I) to treat HIV. In addition, there is no proof that the claimed compounds have ever been administered to a human or to an animal model. The obstacles to therapeutic approaches and vaccine development with

regard to retroviruses associated with AIDS in humans are well documented in the literature. See, for example, Huff {J. Med. Chem. 34(8) 1991, p. 2305-2314} on page 2314. These obstacles include and are not limited to : 1) the extensive genomic diversity associated with HIV, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a convert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to traverse the blood brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting therapeutic regimen on its face. In addition, there is no established correlation between in vitro activity and accomplishing treatment of viral infections, especially HIV infections, in vivo, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use the compounds of the formula (I) since there is no description of an actual method wherein a viral infection in a host is treated.

Applicants claimed compounds useful in medical therapy also includes the treatment of cancers. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based

primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531) Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the inhibition of AKT and ERK one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims due to the unpredictability of the role the inhibition of AKT and ERK and, for example, since it is known that there is no known cure for Alzheimer's disease and treatment protocols for Alzheimer's disease depend on the stage of the disease.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of diseases applicant considers as treatable by the inhibition of ERK and AKT found on

pages 50-53, 45 and 46. There are no working examples present for the treatment of any specific disease or disorder.

Test assays and procedure are provided in the specification at pages 58-63 for only AKT3 and ERK2. However, the disclosure does not provide how this in vitro data correlates to the treatment of the assorted list of disorders of the instant claims.

Further, there is no disclosure regarding how all types of the diseases having divers mechanisms are treated. Receptor activity is generally unpredictable and a highly structure specific area, and the data provided of is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

There is also no disclosure as to how the various types of autoimmune, cardiovascular, inflammatory, etc. disorders are treated or prevented.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is the inhibition of any AKT and ERK and the treatment of diseases such as cancer, stroke, diabetes, hepatomegaly, cardiovascular disease,

Alzheimer's disease, cystic fibrosis, viral disease, autoimmune diseases, atherosclerosis, restenosis, psoriasis, allergic disorders, inflammation, neurological disorders, a hormone-related disease, conditions associated with organ transplantation, immunodeficiency disorders, destructive bone disorders, proliferative disorders, infectious diseases, conditions associated with cell death, thrombin-induced platelet aggregation, chronic myelogenous leukemia (CML), liver disease, or pathologic immune conditions involving T cell activation, etc.. Furthermore, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

The disorders encompassed by the instant claims include, for example, inflammatory and cardiovascular disorders such as Alzheimer's disease and stroke, etc. some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited (treated) by the inhibition of AKT or ERK and would furthermore then have to determine which of the claimed compounds would provide treatment of which disease, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the inhibit on of ERK and AKT and the treatment of diseases such as cancer, stroke, diabetes, hepatomegaly, cardiovascular disease, Alzheimer's disease, cystic fibrosis, viral disease, autoimmune diseases, atherosclerosis, restenosis, psoriasis, allergic disorders, inflammation, neurological disorders, a hormone-related disease, conditions associated with organ transplantation, immunodeficiency disorders, destructive bone disorders, proliferative disorders, infectious diseases, conditions associated with cell death, thrombin-induced platelet aggregation, chronic myelogenous leukemia (CML), liver disease, or pathologic immune conditions involving T cell activation as a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention. (Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the

instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the method claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number: 10/626,356
Art Unit: 1626

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Rebecca Anderson
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600
7/19/06

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

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	B	US-			
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	D	US-			
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	F	US-			
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	X	Cancer and Metastasis Reviews (1998), 17(1), 91-106.

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
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